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Bemerkungen:

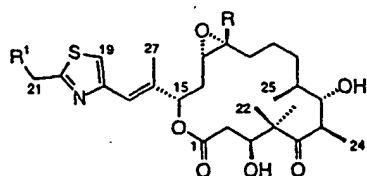
Diese Anmeldung ist am 08 - 10 - 2002 als
Teilanmeldung zu der unter INID-Kode 62
erwähnten Anmeldung eingereicht worden.

(54) **Epothilon-Nebenkomponenten**

(57) Die Erfindung betrifft Verbindungen, die durch Fermentation von DSM 6773 erhältlich sind, insbesondere Epothilone A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3 I4, I5, I6 und K und Trans-Epothilone C1 und C2.

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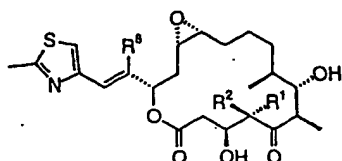


Epothilone A (1) $R^1 = H$; $R = H$

Epothilone B (2) $R^1 = H$; $R = Me$

Epothilone E (3) $R^1 = OH$; $R = H$

Epothilone F (4) $R^1 = OH$; $R = Me$

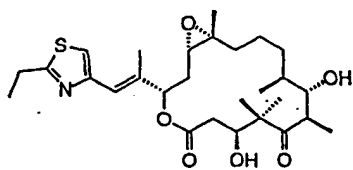


Epothilone A₁ (5) $R^1 = H$; $R^2, R^8 = Me$

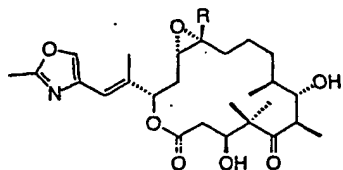
Epothilone A₂ (6) $R^2 = H$; $R^1, R^8 = Me$

Epothilone A₈ (7) $R^8 = H$; $R^1, R^2 = Me$

Epothilone A₉ (8) $R^1 = CH_2OH$; $R^2, R^8 = Me$

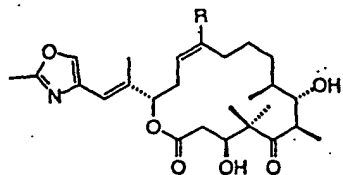


Epothilone B₁₀ (9)



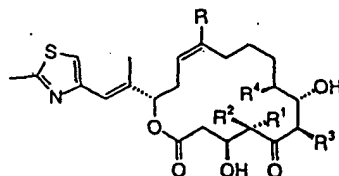
Epothilone G₁ (10) $R = H$

Epothilone G₂ (11) $R = Me$



Epothilone H₁ (12) $R = H$

Epothilone H₂ (13) $R = Me$



Epothilone C (14) $R^1, R^2, R^3, R^4 = Me$; $R = H$

Epothilone D (15) $R^1, R^2, R^3, R^4, R = Me$

Epothilone C₁ (16) $R^1 = H$; $R^2, R^3, R^4 = Me$; $R = H$

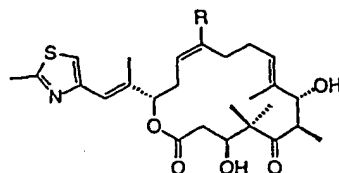
Epothilone D₁ (17) $R^1 = H$; $R^2, R^3, R^4 = Me$; $R = Me$

Epothilone C₂ (18) $R^2 = H$; $R^1, R^3, R^4 = Me$; $R = H$

Epothilone D₂ (19) $R^2 = H$; $R^1, R^3, R^4 = Me$; $R = Me$

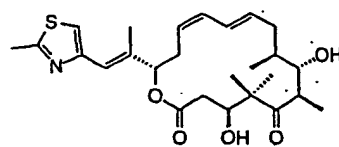
Epothilone C₃ (20) $R^3 = H$; $R^1, R^2, R^4 = Me$; $R = H$

Epothilone C₄ (21) $R^4 = H$; $R^1, R^2, R^3 = Me$; $R = H$

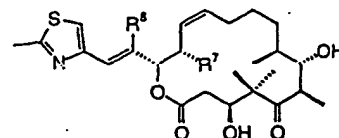


Epothilone C₅ (22) $R = H$

Epothilone D₅ (23) $R = Me$



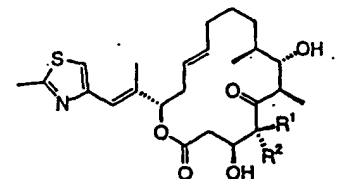
Epothilone C₆ (24)



Epothilone C₇ (25) $R^7 = OH$; $R^8 = Me$

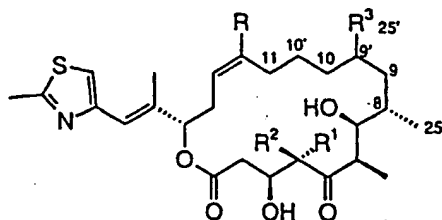
Epothilone C₈ (26) $R^8, R^7 = H$

Epothilone C₉ (27) $R^8 = CH_2OH$; $R^7 = H$



trans-Epothilone C₁ (28) $R^1 = H$; $R^2 = Me$

trans-Epothilone C₂ (29) $R^2 = H$; $R^1 = Me$



Epothilone I₁ (30) R, R³ = H; R¹, R² = Me

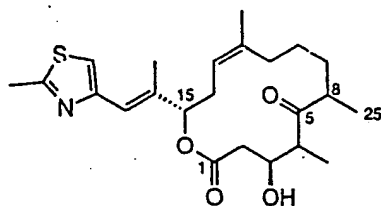
Epothilone I₂ (31) R = H; R¹, R², R³ = Me

Epothilone I₃ (32) R¹, R², R³, R = Me

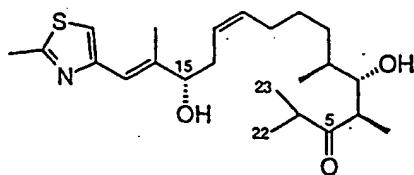
Epothilone I₄ (33) R², R = H; R¹, R³ = Me

Epothilone I₅ (34) R² = H; R¹, R³, R = Me

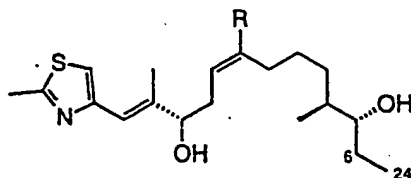
Epothilone I₆ (35) R¹ = H; R², R³, R = Me



Epothilone K (36)



(37)



(38) R = H

(39) R = Me

[0003] Epothilone A₁ (5): colorless amorphous solid; $[\alpha]^{22}_D$ -69 (c 0.1, MeOH); UV (MeOH) λ_{max} nm (ϵ) 208 (19600), 247 (13600); IR (KBr) ν_{max} 3437, 2959, 2931, 2876, 1732, 1710, 1455, 1259, 978 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 6.95 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.68 (1H, dd, J = 4.4, 4.0 Hz, H-15), 4.12 (1H, m, H-3), 3.71 (1H, m, H-7), 3.52 (1H, bs, 7-OH), 3.37 (1H, bd, J = 7.5 Hz, 3-OH), 3.21 (1H, dq, J = 7.7, 7.0 Hz, H-4), 3.02 (1H, ddd, J = 9.2, 4.5, 2.8 Hz, H-13), 2.87 (1H, ddd, J = 8.3, 4.5, 3.7 Hz, H-12), 2.78 (1H, dd, J = 16.8, 4.3 Hz, H-2a), 2.70 (3H, s, H-21), 2.66 (1H, dq, J = 3.9, 7.0 Hz, H-6), 2.65 (1H, dd, J = 16.8, 5.2 Hz, H-2b), 2.16 (1H, ddd, J = 15.4, 4.4, 2.8 Hz, H-14a), 2.12 (3H, bs, H-27), 1.91 (1H, ddd, J = 15.4, 9.2, 4.0 Hz, H-14b), 1.63 (1H, m, H-10a), 1.62 (2H, m, H-11), 1.59 (1H, m, H-9a), 1.52 (1H, m, H-10b), 1.39 (1H, m, H-8), 1.35 (1H, m, H-9b), 1.211 (3H, d, J = 7.0 Hz, H-23), 1.207 (3H, d, J = 7.0 Hz, H-24), 0.89 (3H, d, J = 6.9 Hz, H-25); EIMS m/z 479 $[M]^+$ (21), 322 (31), 306 (65), 304 (47), 168 (45), 166 (73), 164 (100), 151 (30), 140 (35); HREIMS m/z 479.2317 (calcd. for $C_{27}H_{41}NO_5S$, 479.2342).

[0004] Epothilone A₂ (6): colorless amorphous solid; $[\alpha]^{22}_D$ +12.0 (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 210 (15100), 248 (15500); IR (KBr) ν_{max} 3438, 2963, 2929, 2875, 1734, 1706, 1458, 1262, 981 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 6.98 (1H, s, H-19), 6.63 (1H, bs, H-17), 5.40 (1H, dd, J = 8.3, 3.4 Hz, H-15), 4.26 (1H, ddd, J = 8.5, 4.8, 4.7 Hz, H-3), 3.85 (1H, dd, J = 7.9, 2.6 Hz, H-7), 3.54 (1H, bs, 3-OH), 3.09 (1H, dq, J = 4.8, 7.0 Hz, H-4), 3.01 (1H, ddd, J = 8.3, 4.8, 4.6 Hz, H-13), 2.98 (1H, dq, J = 7.9, 7.0 Hz, H-6), 2.89 (1H, ddd, J = 6.7, 4.6, 4.4 Hz, H-12), 2.68 (3H, s, H-21), 2.60 (1H, dd, J = 15.1, 8.5 Hz, H-2a), 2.52 (1H, bs, 7-OH), 2.50 (1H, dd, J = 15.1, 4.7 Hz, H-2b), 2.18 (1H, ddd, J = 15.0, 4.8, 3.4 Hz, H-14a), 2.11 (3H, d, J = 1.3 Hz, H-27), 1.82 (1H, ddd, J = 15.0, 8.3, 8.1 Hz, H-14b), 1.63 (1H, m, H-8), 1.61 (2H, m, H-11a and H-10a), 1.46 (1H, m, H-11b), 1.39 (2H, m, H-9), 1.31 (1H, m, H-10b), 1.22 (3H, d, J = 7.0 Hz, H-24), 1.15 (3H, d, J = 7.0 Hz, H-22), 1.01 (3H, d, J = 6.9 Hz, H-25); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 216.2 (s, C-5), 170.1 (s, C-1), 164.9 (s, C-20), 152.0 (s, C-18), 137.0 (s, C-16), 120.3 (d, C-17), 116.5 (d, C-19), 76.7 (d, C-15), 75.6 (d, C-7), 69.1 (d, C-3), 57.1 (d, C-12), 54.3 (d, C-13), 50.3 (d, C-4), 49.6 (d, C-6), 39.4 (t, C-2), 35.5 (d, C-8), 32.2 (t, C-14), 29.6 (t, C-9), 27.6 (t, C-11), 23.9 (t, C-10), 19.2 (q, C-21), 18.0 (q, C-25), 15.6 (q, C-27), 13.9 (q, C-24), 12.4 (q, C-22); EIMS m/z 479 $[M]^+$ (18), 322 (38), 306 (78), 304 (59), 168 (48), 166 (96), 164 (100), 151 (33), 140 (38); HREIMS m/z 479.2318 (calcd. for $C_{27}H_{41}NO_5S$, 479.2342).

[0005] Epothilone A₈ (7): colorless amorphous solid; $[\alpha]^{22}_D$ -76.2 (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 210 (15300), 248 (15500); IR (KBr) ν_{max} 3440, 2967, 2932, 2876, 1736, 1691, 1467, 1252, 979 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 6.95 (1H, s, H-19), 6.64 (1H, dd, J = 15.6, 0.9 Hz, H-17), 6.52 (1H, dd, J = 15.6, 6.6 Hz, H-16), 5.68 (1H, dddd, J = 7.8, 6.6, 3.2, 0.9 Hz, H-15), 4.11 (1H, ddd, J = 10.1, 6.6, 3.5 Hz, H-3), 3.78 (1H, ddd, J = 5.2, 3.2, 3.2 Hz, H-7), 3.66 (1H, d, J = 6.6 Hz, 3-OH), 3.23 (1H, dq, J = 5.2, 6.9 Hz, H-6), 3.08 (1H, ddd, J = 7.3, 5.5, 4.1 Hz, H-13), 2.90 (1H, ddd, J = 6.6, 4.6, 4.1 Hz, H-12), 2.69 (3H, s, H-21), 2.52 (1H, dd, J = 14.7, 10.1 Hz, H-2a), 2.44 (1H, bd, J = 3.2 Hz, 7-OH), 2.41 (1H, dd, J = 14.7, 3.5 Hz, H-2b), 2.10 (1H, ddd, J = 15.0, 5.5, 3.2 Hz, H-14a), 1.90 (1H, ddd, J = 15.0, 7.8, 7.3 Hz, H-14b), 1.71 (1H, m, H-8), 1.65 (1H, m, H-11a), 1.50 (1H, m, H-10a), 1.47 (1H, m, H-11b), 1.40 (2H, m, H-9), 1.39 (1H, m, H-10b), 1.33 (3H, s, H-23), 1.16 (3H, d, J = 6.9 Hz, H-24), 1.08 (3H, s, H-22), 0.98 (3H, d, J = 7.0 Hz, H-25); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 220.3 (s, C-5), 170.7 (s, C-1), 166.5 (s, C-20), 152.2 (s, C-18), 128.4 (d, C-16), 125.9 (d, C-17), 116.4 (d, C-19), 75.0 (d, C-7), 73.6 (d, C-3), 72.7 (d, C-15), 57.3 (d, C-12), 54.1 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.9 (t, C-2), 36.3 (d, C-8), 32.5 (t, C-14), 30.3 (t, C-9), 26.7 (t, C-11), 24.0 (t, C-10), 21.3 (q, C-23), 21.0 (q, C-22), 19.3 (q, C-21), 17.1 (q, C-25), 14.5 (q, C-24); EIMS m/z 479 $[M]^+$ XXX; HRDCIMS m/z 480.2401 (calcd. for $C_{25}H_{38}NO_6S$, 480.2401).

[0006] Epothilone A₉ (8): colorless amorphous solid; $[\alpha]^{22}_D$ -37.6 (c 0.5, MeOH); UV (MeOH) λ_{max} nm (ϵ) 211

- (15500), 253 (14100); IR (KBr) ν_{\max} 3423, 2965, 2932, 2877, 1736, 1690, 1463, 1249, 1014, 979 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.10 (1H, s, H-19), 6.72 (1H, dd, J = 10.7, 4.3 Hz, 27-OH), 6.60 (1H, bs, H-17), 5.69 (1H, dd, J = 11.6, 2.0 Hz, H-15), 5.59 (1H, d, J = 6.6 Hz, 3-OH), 4.49 (1H, ddd, J = 12.9, 4.3, 1.2 Hz, H-27a), 4.27 (1H, ddd, J = 11.6, 6.6, 2.9 Hz, H-3), 4.11 (1H, ddd, J = 12.9, 10.7, 1.0 Hz, H-27b), 3.71 (1H, ddd, J = 4.8, 3.0, 2.8 Hz, H-7), 3.17 (1H, dq, J = 3.0, 6.8 Hz, H-6), 3.04 (1H, ddd, J = 9.7, 3.6, 2.2 Hz, H-13), 2.93 (1H, bs, 7-OH), 2.91 (1H, ddd, J = 9.7, 3.6, 2.7 Hz, H-12), 2.72 (3H, s, H-21), 2.48 (1H, dd, J = 14.2, 11.6 Hz, H-2a), 2.11 (1H, dd, J = 14.2, 2.9 Hz, H-2b), 2.03 (1H, ddd, J = 14.7, 2.2, 2.0 Hz, H-14a), 1.86 (1H, m, H-11a), 1.85 (1H, m, H-14b), 1.79 (1H, m, H-8), 1.52 (1H, m, H-10a), 1.37 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.36 (1H, in, H-11b), 1.19 (3H, d, J = 6.8 Hz, H-24), 1.02 (3H, d, J = 7.1 Hz, H-25), 1.00 (3H, s, H-22); ^{13}C NMR (CDCl_3 , 75 MHz) δ 220.5 (s, C-5), 170.2 (s, C-1), 167.5 (s, C-20), 150.7 (s, C-18), 138.9 (s, C-16), 125.2 (d, C-17), 119.5 (d, C-19), 76.7 (d, C-15), 73.4 (d, C-7), 70.4 (d, C-3), 57.7 (d, C-12), 57.2 (t, C-27), 55.3 (d, C-13), 54.2 (s, C-4), 41.3 (d, C-6), 40.7 (t, C-2), 37.5 (d, C-8), 31.8 (t, C-14), 31.2 (t, C-9), 28.0 (t, C-11), 23.7 (q, C-23), 23.2 (t, C-10), 19.2 (q, C-21), 16.8 (q, C-22), 15.8 (q, C-25), 13.5 (q, C-24); EIMS m/z 509 $[\text{M}]^+$ (9), 491 (4), 322 (28), 321 (25), 180 (45), 167 (40), 166 (100), 165 (49), 154 (47), 138 (33); HREIMS m/z 509.2467 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_7\text{S}$, 509.2447).
- [0007] Epothilone B₁₀ (9):** colorless amorphous solid; $[\alpha]_D^{25}$ -27 (c 0.15, MeOH); UV (MeOH) λ_{\max} nm (ε) 212 (15800), 247 (12500); IR (KBr) ν_{\max} 3434, 2962, 2930, 2876, 2858, 1733, 1692, 1461, 1259, 1052, 981 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 6.99 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.42 (1H, dd, J = 8.0, 3.0 Hz, H-15), 4.25 (1H, ddd, J = 9.5, 6.3, 2.8 Hz, H-3), 4.23 (1H, bs, 3-OH), 3.77 (1H, ddd, J = 4.0, 3.9, 3.8 Hz, H-7), 3.30 (1H, dq, J = 4.0, 6.9 Hz, H-6), 3.01 (2H, q, J = 7.6 Hz, H-21), 2.81 (1H, dd, J = 7.7, 4.6 Hz, H-13), 2.68 (1H, bs, 7-OH), 2.54 (1H, dd, J = 13.9, 9.5 Hz, H-2a), 2.36 (1H, dd, J = 13.9, 2.8 Hz, H-2b), 2.11 (1H, ddd, J = 15.3, 4.6, 3.0 Hz, H-14a), 2.09 (3H, s, H-27), 1.91 (1H, ddd, J = 15.3, 8.0, 7.7 Hz, H-14b), 1.74 (1H, m, H-8), 1.73 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.41 (1H, m, H-11b), 1.39 (3H, t, J = 7.6 Hz, H-28), 1.38 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.28 (3H, s, H-26), 1.17 (3H, d, J = 6.9 Hz, H-24), 1.09 (3H, s, H-22), 1.01 (3H, d, J = 7.0 Hz, H-25); EIMS m/z 521 $[\text{M}]^+$ (22), 449 (7), 350 (18), 334 (57), 248 (16), 234 (27), 196 (41), 182 (59), 180 (96), 178 (100), 166 (44), 154 (44); HREIMS m/z 521.2808 (calcd. for $\text{C}_{28}\text{H}_{43}\text{NO}_6\text{S}$, 521.2811).
- [0008] Epothilone G₁ (10):** colorless amorphous solid; $[\alpha]_D^{25}$ -39.7 (c 1.0, MeOH); UV (MeOH) λ_{\max} nm (ε) 203 (15200), 236 (15100); IR (KBr) ν_{\max} 3456, 2962, 2933, 2876, 1736, 1691, 1585, 1466, 1262, 980 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.47 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.42 (1H, dd, J = 8.3, 2.9 Hz, H-15), 4.11 (1H, ddd, J = 10.1, 6.1, 3.4 Hz, H-3), 3.78 (1H, bddd, J = 5.2, 3.5, 3.5 Hz, H-7), 3.63 (1H, bd, J = 6.1 Hz, 3-OH), 3.21 (1H, dq, J = 5.2, 7.0 Hz, H-6), 3.00 (1H, ddd, J = 7.7, 4.8, 4.2 Hz, H-13), 2.88 (1H, ddd, J = 7.1, 4.2, 4.2 Hz, H-12), 2.53 (1H, dd, J = 14.8, 10.1 Hz, H-2a), 2.51 (1H, bd, J = 3.5 Hz, 7-OH), 2.43 (1H, dd, J = 14.8, 3.4 Hz, H-2b), 2.43 (3H, s, H-21), 2.07 (1H, ddd, J = 15.1, 4.8, 2.9 Hz, H-14a), 1.99 (3H, d, J = 1.3 Hz, H-27), 1.86 (1H, ddd, J = 15.1, 8.3, 7.7 Hz, H-14b), 1.71 (1H, m, H-8), 1.69 (1H, m, H-11a), 1.53 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.40 (3H, m, H-9 and H-10b), 1.34 (3H, s, H-23), 1.16 (3H, d, J = 7.0 Hz, H-24), 1.09 (3H, s, H-22), 0.99 (3H, d, J = 6.9 Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 220.1 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.7 (s, C-16), 135.9 (d, C-19), 116.4 (d, C-17), 76.4 (d, C-15), 74.9 (d, C-7), 73.7 (d, C-3), 57.4 (d, C-12), 54.4 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.8 (t, C-2), 36.2 (d, C-8), 31.4 (t, C-14), 30.4 (t, C-9), 27.0 (t, C-11), 23.9 (t, C-10), 21.3 (q, C-23), 21.2 (q, C-22), 17.2 (q, C-25), 15.8 (q, C-27), 14.4 (q, C-24), 13.8 (q, C-21); EIMS m/z 477 $[\text{M}]^+$ (4), 405 (7), 290 (40), 152 (39), 150 (100), 148 (23), 124 (23); HREIMS m/z 477.2684 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_7$, 477.2727).
- [0009] Epothilone G₂ (11):** colorless amorphous solid; $[\alpha]_D^{25}$ -22.6 (c 1.0, MeOH); UV (MeOH) λ_{\max} nm (ε) 202 (21500), 236 (14800); IR (KBr) ν_{\max} 3456, 2965, 2934, 2877, 1737, 1690, 1586, 1464, 1250, 980 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.48 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.43 (1H, dd, J = 7.1, 3.6 Hz, H-15), 4.12 (1H, ddd, J = 9.9, 6.4, 3.4 Hz, H-3), 3.77 (1H, ddd, J = 4.7, 4.4, 4.1 Hz, H-7), 3.83 (1H, bd, J = 6.4 Hz, 3-OH), 3.30 (1H, dq, J = 4.7, 6.9 Hz, H-6), 2.78 (1H, dd, J = 7.0, 5.4 Hz, H-13), 2.54 (1H, dd, J = 14.3, 9.9 Hz, H-2a), 2.51 (1H, bd, J = 4.1 Hz, 7-OH), 2.44 (3H, s, H-21), 2.40 (1H, dd, J = 14.3, 3.4 Hz, H-2b), 2.03 (1H, ddd, J = 15.2, 5.4, 3.6 Hz, H-14a), 2.00 (3H, d, J = 1.3 Hz, H-27), 1.92 (1H, ddd, J = 15.1, 7.1, 7.0 Hz, H-14b), 1.71 (1H, m, H-8), 1.68 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.39 (3H, m, H-9 and H-10b), 1.35 (3H, s, H-23), 1.26 (3H, s, H-26), 1.16 (3H, d, J = 6.9 Hz, H-24), 1.07 (3H, s, H-22), 0.99 (3H, d, J = 7.0 Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 220.7 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.5 (s, C-16), 135.9 (d, C-19), 116.3 (d, C-17), 76.6 (d, C-15), 74.6 (d, C-7), 73.5 (d, C-3), 61.3 (s, C-12), 61.1 (d, C-13), 52.7 (s, C-4), 43.4 (d, C-6), 39.0 (t, C-2), 36.5 (d, C-8), 32.0 (t, C-11), 31.8 (t, C-14), 30.8 (t, C-9), 22.8 (t, C-10), 22.9 (q, C-26), 21.0 (q, C-23), 20.8 (q, C-22), 17.2 (q, C-25), 15.9 (q, C-27), 14.1 (q, C-24), 13.8 (q, C-21); EIMS m/z 491 $[\text{M}]^+$ (21), 419 (6), 320 (18), 304 (39), 166 (42), 152 (57), 150 (100), 149 (44), 148 (58), 124 (35), 109 (33); HREIMS m/z 491.2878 (calcd. for $\text{C}_{27}\text{H}_{41}\text{NO}_7$, 491.2883).
- [0010] Epothilone H₁ (12):** colorless amorphous solid; $[\alpha]_D^{25}$ -84.2 (c 0.2, MeOH); UV (MeOH) λ_{\max} nm (ε) 203 (19600), 237 (12000); IR (KBr) ν_{\max} 3436, 2933, 2880, 2860, 1734, 1688, 1585, 1251, 1007 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.47 (1H, s, H-19), 6.31 (1H, bs, H-17), 5.43 (1H, ddd, J = 10.6, 10.2, 4.5 Hz, H-12), 5.36 (1H, dddd, J = 10.6, 9.6, 5.0, 1.3 Hz, H-13), 5.30 (1H, dd, J = 9.9, 2.0 Hz, H-15), 4.16 (1H, ddd, J = 11.2, 5.3, 2.8 Hz, H-3), 3.73 (1H, ddd, J = 3.9, 2.5, 2.3 Hz, H-7), 3.12 (1H, dq, J = 2.3, 6.9 Hz, H-6), 2.92 (1H, d, J = 2.5 Hz, 7-OH), 2.91 (1H, d, J = 5.3

- H_z, 7-OH), 2.66 (1H, ddd, $J = 15.1, 9.9, 9.6$ Hz, H-14a), 2.50 (1H, dd, $J = 15.4, 11.2$ Hz, H-2a), 2.43 (3H, s, H-21), 2.37 (1H, dd, $J = 15.4, 2.8$ Hz, H-2b), 2.23 (1H, m, H-14b), 2.18 (1H, m, H-11a), 2.01 (1H, m, H-11b), 2.08 (3H, d, $J = 1.3$ Hz, H-27), 1.74 (1H, m, H-8), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-9a), 1.31 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.17 (3H, d, $J = 6.9$ Hz, H-24), 1.08 (3H, s, H-22), 0.99 (3H, d, $J = 7.1$ Hz, H-25); ¹³C NMR, see Table 1; EIMS m/z 461 [M]⁺ (6), 310 (5), 274 (10), 273 (7), 171 (63), 152 (100), 148 (18), 111 (15); HREIMS m/z 461.2743 (calcd. for C₂₆H₃₉NO₆, 461.2777).
- [0011] Epothilone H₂ (13):** colorless amorphous solid; $[\alpha]_D^{22} -44.4$ (c 0.25, MeOH); UV (MeOH) λ_{max} nm (ϵ) 203 (14500), 236 (12200); IR (KBr) ν_{max} 3436, 2967, 2935, 2880, 1734, 1690, 1586, 1251, 1007 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.46 (1H, s, H-19), 6.30 (1H, bs, H-17), 5.23 (1H, dd, $J = 9.8, 2.1$ Hz, H-15), 5.12 (1H, dd, $J = 10.1, 5.3$ Hz, H-13), 4.20 (1H, ddd, $J = 10.8, 5.7, 2.9$ Hz, H-3), 3.71 (1H, ddd, $J = 3.8, 2.6, 2.6$ Hz, H-7), 3.14 (1H, dq, $J = 2.6, 6.9$ Hz, H-6), 2.93 (d, $J = 5.7$ Hz, 3-OH), 2.90 (1H, bd, $J = 2.6$ Hz, 7-OH), 2.62 (1H, ddd, $J = 15.1, 9.8, 9.8$ Hz, H-14a), 2.46 (1H, dd, $J = 15.1, 10.8$ Hz, H-2a), 2.43 (3H, s, H-21), 2.32 (1H, dd, $J = 15.1, 2.9$ Hz, H-2b), 2.29 (1H, m, H-11a), 2.19 (1H, bd, $J = 15.1$ Hz, H-14b), 1.97 (3H, d, $J = 1.3$ Hz, H-27), 1.87 (1H, m, H-11b), 1.73 (1H, m, H-8), 1.67 (1H, m, H-10a), 1.65 (3H, bs, H-26), 1.32 (3H, s, H-23), 1.26 (2H, m, H-9), 1.24 (1H, m, H-10b), 1.18 (3H, d, $J = 6.9$ Hz, H-24), 1.07 (3H, s, H-22), 1.00 (3H, d, $J = 7.0$ Hz, H-25); ¹³C NMR (CDCl₃, 100 MHz) δ 220.6 (s, C-5), 170.3 (s, C-1), 161.0 (s, C-20), 138.6 (s, C-12), 138.4 (s, C-16), 137.5 (s, C-18), 135.6 (d, C-19), 120.8 (d, C-13), 115.8 (d, C-17), 78.9 (d, C-15), 74.3 (d, C-7), 72.7 (d, C-3), 53.3 (s, C-4), 42.0 (d, C-6), 39.6 (t, C-2), 38.6 (d, C-8), 32.4 (t, C-14), 31.9 (t, C-9), 31.6 (t, C-11), 25.6 (t, C-10), 23.0 (q, C-26), 22.8 (q, C-23), 18.8 (q, C-22), 16.1 (q, C-27), 15.9 (q, C-25), 13.8 (q, 0.21), 13.6 (q, C-24); EIMS m/z 475 [M]⁺ (11), 288 (9), 287 (5), 188 (7), 171 (32), 152 (100), 111 (10); HREIMS m/z 475.2913 (calcd. for C₂₇H₄₁NO₆, 475.2934).
- [0012] Epothilone C₁ (16):** colorless amorphous solid; $[\alpha]_D^{22} -114.0$ (c 10.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 211 (16500), 248 (12500); IR (KBr) ν_{max} 3440, 2933, 2877, 2858, 1730, 1708, 1457, 1244, 981 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 6.96 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.47 (1H, dd, $J = 9.2, 3.0$ Hz, H-15), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 4.40 (1H, ddd, $J = 6.2, 6.1, 6.1$ Hz, H-3), 3.69 (1H, dd, $J = 5.7, 3.6$ Hz, H-7), 3.01 (1H, dq, $J = 5.7, 6.9$ Hz, H-6), 3.01 (1H, bs, 3-OH), 2.84 (1H, dq, $J = 5.2, 7.0$ Hz, H-4), 2.68 (3H, s, H-21), 2.66 (1H, ddd, $J = 16.4, 9.2, 7.3$ Hz, H-14a), 2.64 (1H, dd, $J = 15.9, 7.1$ Hz, H-2a), 2.54 (1H, dd, $J = 15.9, 6.1$ Hz, H-2b), 2.38 (1H, bd, $J = 16.4$ Hz, H-14b), 2.35 (1H, bs, 7-OH), 2.07 (3H, bs, H-27), 2.03 (2H, m, H-11), 1.62 (1H, m, H-10a), 1.53 (1H, m, H-8), 1.35 (1H, m, H-9a), 1.22 (1H, m, H-9b), 1.19 (3H, d, $J = 6.9$ Hz, H-24), 1.14 (3H, d, $J = 6.9$ Hz, H-23), 1.10 (1H, m, H-10b), 0.95 (3H, d, $J = 6.9$ Hz, H-25); ¹³C NMR, see Table 1; EIMS m/z 463 [M]⁺ (5), 324 (8), 290 (8), 204 (7), 168 (100), 164 (15), 139 (36); HREIMS m/z 463.2381 (calcd. for C₂₅H₃₇NO₅S, 463.2392).
- [0013] Epothilone D₁ (17):** colorless amorphous solid; $[\alpha]_D^{22} -118.6$ (c 0.5, MeOH); UV (MeOH) λ_{max} nm (ϵ) 208 (18300), 249 (11900); IR (KBr) ν_{max} 3439, 2965, 2934, 2877, 1729, 1707, 1456, 1250, 980 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 6.98 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.51 (1H, dd, $J = 9.5, 3.4$ Hz, H-15), 5.16 (1H, dd, $J = 8.0, 4.2$ Hz, H-13), 4.42 (1H, ddd, $J = 7.1, 6.3, 5.5$ Hz, H-3), 3.70 (1H, dd, $J = 6.5, 2.9$ Hz, H-7), 3.07 (1H, dq, $J = 6.5, 6.9$ Hz, H-6), 2.95 (1H, dq, $J = 4.7, 7.0$ Hz, H-4), 2.71 (3H, s, H-21), 2.69 (1H, dd, $J = 16.0, 6.3$ Hz, H-2a), 2.64 (1H, m, H-14a), 2.59 (1H, dd, $J = 16.0, 7.1$ Hz, H-2b), 2.46 (1H, bs, 3-OH), 2.38 (1H, bd, $J = 16.0$ Hz, H-14b), 2.19 (1H, ddd, $J = 13.3, 8.6, 5.7$ Hz, H-11a), 2.10 (3H, d, $J = 1.4$ Hz, H-27), 2.02 (1H, bs, 7-OH), 1.91 (1H, ddd, $J = 13.3, 6.0, 6.0$ Hz, H-11b), 1.68 (1H, m, H-10a), 1.66 (3H, bs, H-26), 1.53 (1H, m, H-8), 1.37 (1H, m, H-9a), 1.26 (1H, m, H-9b), 1.24 (3H, d, $J = 6.9$ Hz, H-24), 1.19 (1H, m, H-10b), 1.14 (3H, d, $J = 7.0, 7.0$ Hz, H-23), 0.99 (3H, d, $J = 6.9$ Hz, H-25); ¹³C NMR (CDCl₃, 100 MHz) δ 217.0 (s, C-5), 169.7 (s, C-1), 165.0 (s, C-20), 152.2 (s, C-18), 138.5 (s, C-12), 137.7 (s, C-16), 120.7 (d, C-13), 120.1 (d, C-17), 116.3 (d, C-19), 78.8 (d, C-15), 77.2 (d, C-7), 67.7 (d, C-3), 52.1 (d, C-4), 46.5 (d, C-6), 40.6 (t, C-2), 37.6 (d, C-8), 32.3 (t, C-14), 31.8 (t, C-11), 29.5 (t, C-9), 25.5 (t, C-10), 23.1 (q, C-26), 19.2 (q, C-21), 15.5 (q, C-27), 16.6 (q, C-25), 14.5 (q, C-24), 9.7 (q, C-23); EIMS m/z 477 [M]⁺ (13), 304 (19), 303 (31), 218 (40), 204 (41), 168 (100), 164 (45), 157 (25), 139 (18); HREIMS m/z 477.2544 (calcd. for C₂₆H₃₉NO₅S, 477.2549).
- [0014] Epothilone C₂ (18):** colorless amorphous solid; $[\alpha]_D^{22} -11.6$ (c 10.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 212 (15500), 249 (12100); IR (KBr) ν_{max} 3428, 2962, 2929, 2877, 2859, 1734, 1705, 1460, 1251, 982 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 6.99 (1H, s, H-19), 6.66 (1H, bs, H-17), 5.55 (1H, ddd, $J = 10.4, 9.2, 6.1$ Hz, H-12), 5.38 (1H, ddd, $J = 10.4, 9.3, 6.2$ Hz, H-13), 5.22 (1H, dd, $J = 8.8, 2.8$ Hz, H-15), 4.42 (1H, dddd, $J = 9.4, 5.6, 4.2, 4.1$ Hz, H-3), 3.93 (1H, d, $J = 5.6$ Hz, 3-OH), 3.86 (1H, m, H-7), 3.15 (1H, bs, 7-OH), 3.12 (1H, dq, $J = 4.2, 7.0$ Hz, H-4), 3.00 (1H, dq, $J = 6.9, 7.0$ Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dddd, $J = 15.1, 9.3, 8.8, 0.8$ Hz, H-14a), 2.58 (1H, dd, $J = 15.4, 9.4$ Hz, H-2a), 2.38 (1H, dd, $J = 15.4, 4.1$ Hz, H-2b), 2.31 (1H, ddd, $J = 15.1, 6.2, 2.8$ Hz, H-14b), 2.08 (3H, d, $J = 1.3$ Hz, H-27), 2.15 (1H, m, H-11a), 2.04 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.59 (1H, m, H-10a), 1.43 (1H, m, H-9a), 1.31 (1H, m, H-9b), 1.26 (3H, d, $J = 7.0$ Hz, H-24), 1.15 (3H, d, $J = 7.0$ Hz, H-23), 1.11 (1H, m, H-10b), 1.00 (3H, d, $J = 6.9$ Hz, H-25); ¹³C NMR, see Table 1; EIMS m/z 463 [M]⁺ (7), 324 (7), 306 (8), 290 (17), 168 (100), 164 (14), 139 (27); HREIMS m/z 463.2392 (calcd. for C₂₅H₃₇NO₅S, 463.2392).
- [0015] Epothilone D₂ (19):** colorless amorphous solid; $[\alpha]_D^{22} -12.5$ (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 210 (15400), 248 (11200); IR (KBr) ν_{max} 3436, 2965, 2930, 2877, 1732, 1705, 1458, 1253, 980 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 6.97 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.18 (1H, dd, $J = 7.9, 4.9$ Hz, H-15), 5.18 (1H, ddd, $J = 9.6, 5.4, 1.0$ Hz,

H-13), 4.27 (1H, m, H-3), 3.88 (1H, dd, $J = 5.6, 4.6$ Hz, H-7), 3.19 (1H, bs, 3-OH), 3.07 (1H, dq, $J = 4.3, 7.0$ Hz, H-4), 2.95 (1H, dq, $J = 5.6, 7.0$ Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd, $J = 14.9, 7.8$ Hz, H-2a), 2.56 (1H, ddd, $J = 14.7, 9.6, 7.9$ Hz, H-14a), 2.43 (1H, dd, $J = 14.9, 5.6$ Hz, H-2b), 2.38 (1H, bs, 7-OH), 2.26 (1H, ddd, $J = 14.5, 5.4, 4.9$ Hz, H-14b), 2.19 (1H, ddd, $J = 13.0, 10.4, 5.4$ Hz, H-11a), 2.10 (3H, d, $J = 1.4$ Hz, H-27), 1.95 (1H, ddd, $J = 13.0, 10.3, 5.3$ Hz, H-11b), 1.72 (1H, m, H-8), 1.68 (3H, bs, H-26), 1.61 (1H, m, H-10a), 1.39 (2H, m, H-9), 1.21 (1H, m, H-10b), 1.19 (3H, d, $J = 6.9$ Hz, H-24), 1.17 (3H, d, $J = 7.0, 7.0$ Hz, H-22), 1.00 (3H, d, $J = 6.9$ Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 216.8 (s, C-5), 170.4 (s, C-1), 164.9 (s, C-20), 152.3 (s, C-18), 139.8 (s, C-12), 137.5 (s, C-16), 120.5 (d, C-17), 119.2 (d, C-13), 116.3 (d, C-19), 80.0 (d, C-15), 74.3 (d, C-7), 69.7 (d, C-3), 48.6 (d, C-4), 48.4 (d, C-6), 39.9 (t, C-2), 36.6 (d, C-8), 32.2 (t, C-14), 32.7 (t, C-11), 30.9 (t, C-9), 26.0 (t, C-10), 23.6 (q, C-26), 19.2 (q, C-21), 15.4 (q, C-27), 17.1 (q, C-25), 12.4 (q, C-24), 12.7 (q, C-23); EIMS m/z 477 $[\text{M}]^+$ (22), 304 (19), 303 (17), 218 (22), 204 (25), 168 (100), 164 (28), 157 (31), 139 (21); HREIMS m/z 477.2545 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_5\text{S}$, 477.2549).

[0016] Epothilone C₃ (20): colorless amorphous solid; $[\alpha]_D^{22} -62.1$ (c 5.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 212 (16200), 248 (12300); IR (KBr) ν_{max} 3432, 2928, 2878, 2858, 1736, 1698, 1252, 1040 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.95 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.44 (1H, ddd, $J = 10.9, 10.3, 5.4$ Hz, H-12), 5.33 (1H, ddd, $J = 10.9, 9.3, 4.6$ Hz, H-13), 5.23 (1H, dd, $J = 9.5, 2.2$ Hz, H-15), 4.36 (1H, ddd, $J = 11.3, 5.6, 2.3$ Hz, H-3), 4.04 (1H, d, $J = 5.6$ Hz, 3-OH), 3.93 (1H, ddd, $J = 9.5, 2.3, 1.4$ Hz, H-7), 3.56 (1H, bd, $J = 2.3$ Hz, 7-OH), 2.70 (1H, dd, $J = 18.0, 1.4$ Hz, H-6a), 2.67 (3H, s, H-21), 2.61 (1H, ddd, $J = 15.3, 9.5, 9.3$ Hz, H-14a), 2.38 (1H, dd, $J = 14.3, 11.3$ Hz, H-2a), 2.36 (1H, dd, $J = 18.0, 9.5$ Hz, H-6b), 2.28 (1H, bd, $J = 15.3$ Hz, H-14b), 2.12 (1H, m, H-11a), 2.06 (1H, dd, $J = 14.3, 2.3$ Hz, H-2b), 2.03 (3H, d, $J = 1.3$ Hz, H-27), 1.96 (1H, m, H-11b), 1.75 (1H, m, H-8), 1.54 (1H, m, H-10a), 1.26 (1H, m, H-9a), 1.25 (3H, s, H-23), 1.17 (1H, m, H-10b), 1.15 (1H, m, H-9b), 1.03 (3H, s, H-22), 0.91 (3H, d, $J = 6.8$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (28), 290 (14), 168 (100), 164 (36), 157 (44), 151 (25); HREIMS m/z 463.2379 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

[0017] Epothilone C₄ (21): colorless amorphous solid; $[\alpha]_D^{22} -75.6$ (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 212 (17200), 248 (12500); IR (KBr) ν_{max} 3434, 2974, 2932, 2859, 1735, 1686, 1252, 1046 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.96 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 5.26 (1H, dd, $J = 9.6, 2.3$ Hz, H-15), 4.41 (1H, ddd, $J = 11.4, 5.8, 2.5$ Hz, H-3), 3.78 (1H, m, H-7), 3.70 (1H, bs, 3-OH), 3.46 (1H, d, $J = 0.9$ Hz, 7-OH), 3.01 (1H, dq, $J = 0.5, 7.0$ Hz, H-6), 2.69 (3H, s, H-21), 2.66 (1H, ddd, $J = 15.3, 9.6, 8.8$ Hz, H-14a), 2.47 (1H, dd, $J = 14.5, 11.4$ Hz, H-2a), 2.29 (1H, m, H-14b), 2.25 (1H, dd, $J = 14.5, 2.5$ Hz, H-2b), 2.24 (1H, m, H-11a), 2.07 (3H, d, $J = 1.4$ Hz, H-27), 1.96 (1H, m, H-11b), 1.51 (2H, m, H-8), 1.44 (2H, m, H-10), 1.37 (2H, m, H-9), 1.32 (3H, s, H-23), 1.17 (3H, d, $J = 7.0$ Hz, H-24), 1.07 (3H, s, H-22); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (7), 276 (15), 171 (33), 168 (100), 164 (23), 151 (22), 111 (13); HREIMS m/z 463.2373 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

[0018] Epothilone C₅ (22): colorless amorphous solid; $[\alpha]_D^{22} -158.2$ (c 0.5, MeOH); UV (MeOH) λ_{max} nm (ϵ) 205 (19500), 247 (12700); IR (KBr) ν_{max} 3447, 2972, 2927, 1737, 1690, 1450, 1252, 1181, 986 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.93 (1H, s, H-19), 6.48 (1H, bs, H-17), 5.48 (1H, ddd, $J = 10.7, 6.2, 6.2$ Hz, H-12), 5.39 (1H, m, H-13), 5.37 (1H, m, H-9), 5.34 (1H, dd, $J = 8.0, 2.3$ Hz, H-15), 4.29 (1H, dd, $J = 6.0, 2.6$ Hz, H-7), 4.09 (1H, ddd, $J = 10.8, 7.1, 2.9$ Hz, H-3), 3.59 (1H, d, $J = 7.1$ Hz, 3-OH), 3.17 (1H, dq, $J = 6.0, 6.9$ Hz, H-6), 2.68 (3H, s, H-21), 2.54 (1H, ddd, $J = 15.2, 8.1, 8.0$ Hz, H-14a), 2.44 (1H, bs, 7-OH), 2.42 (1H, dd, $J = 15.1, 2.9$ Hz, H-2a), 2.41 (1H, ddd, $J = 15.2, 2.3, 2.3$ Hz, H-14b), 2.34 (1H, dd, $J = 15.1, 10.8$ Hz, H-2b), 2.20 (1H, m, H-10a), 2.18 (2H, m, H-11), 2.12 (1H, m, H-10b), 2.06 (3H, bs, H-27), 1.67 (3H, bs, H-25), 1.27 (3H, s, H-23), 1.21 (3H, d, $J = 6.9$ Hz, H-24), 1.15 (3H, s, H-22); ^{13}C NMR, see Table 1; EIMS m/z 475 $[\text{M}]^+$ (6), 392 (7), 304 (6), 288 (33), 204 (76), 171 (19), 168 (100), 164 (12); HREIMS m/z 475.2380 (calcd. for $\text{C}_{26}\text{H}_{37}\text{NO}_5\text{S}$, 475.2392).

[0019] Epothilone D₅ (23): colorless amorphous solid; $[\alpha]_D^{22} -150$ (c 0.2, MeOH); UV (MeOH) λ_{max} nm (ϵ) 205 (23300), 248 (13600); IR (KBr) ν_{max} 3439, 2967, 2927, 1736, 1690, 1451, 1254, 1181, 987 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.94 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.34 (1H, bs, H-9), 5.29 (1H, dd, $J = 8.0, 2.4$ Hz, H-15), 5.16 (1H, dd, $J = 8.2, 6.2$ Hz, H-13), 4.30 (1H, bd, $J = 4.9$ Hz, H-7), 4.19 (1H, ddd, $J = 10.8, 7.6, 3.0$ Hz, H-3), 3.68 (1H, d, $J = 7.6$ Hz, 3-OH), 3.17 (1H, dq, $J = 4.9, 7.0$ Hz, H-6), 2.69 (3H, s, H-21), 2.65 (1H, d, $J = 2.1$ Hz, 7-OH), 2.56 (1H, ddd, $J = 16.2, 8.2, 8.0$ Hz, H-14a), 2.40 (1H, dd, $J = 15.0, 3.0$ Hz, H-2a), 2.39 (1H, bd, $J = 16.2$ Hz, H-14b), 2.34 (1H, dd, $J = 15.0, 10.8$ Hz, H-2b), 2.25 (2H, m, H-10a and H-11a), 2.20 (1H, m, H-10b), 2.17 (1H, m, H-11b), 2.05 (3H, d, $J = 1.0$ Hz, H-27), 1.69 (3H, bs, H-25), 1.68 (3H, bs, H-26), 1.29 (3H, s, H-23), 1.23 (3H, d, $J = 7.0$ Hz, H-24), 1.16 (3H, s, H-22); ^{13}C NMR, see Table 1; EIMS m/z 489 $[\text{M}]^+$ (4), 406 (4), 338 (7), 302 (13), 218 (35), 171 (10), 168 (100), 153 (20), 125 (10); HREIMS m/z 489.2536 (calcd. for $\text{C}_{27}\text{H}_{39}\text{NO}_5\text{S}$, 489.2549).

[0020] Epothilone C₆ (24): colorless amorphous solid; $[\alpha]_D^{22} -205.2$ (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 218 (24600), 237 (28800); IR (KBr) ν_{max} 3435, 2967, 2927, 2882, 1732, 1688, 1465, 1258, 988 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.97 (1H, s, H-19), 6.58 (1H, bs, H-17), 6.43 (1H, dd, 15.5, 10.8 Hz, H-11), 6.11 (1H, dd, $J = 10.8, 10.6$ Hz, H-12), 5.75 (1H, ddd, $J = 15.5, 8.3, 5.6$ Hz, H-10), 5.34 (1H, m, H-13), 5.34 (1H, dd, $J = 9.7, 2.4$ Hz, H-15), 4.16 (1H, ddd, $J = 9.2, 4.9, 4.3$ Hz, H-3), 3.74 (1H, ddd, $J = 2.2, 2.1, 1.7$ Hz, H-7), 3.24 (1H, dq, $J = 2.1, 6.9$ Hz, H-6), 3.06 (1H, d, $J = 2.2$ Hz, 7-OH), 2.93 (1H, d, $J = 4.9$ Hz, 3-OH), 2.78 (1H, dddd, $J = 14.1, 9.9, 9.7, 0.7$ Hz, H-14a), 2.71 (3H, s, H-21), 2.48 (1H, m, H-9a), 2.47 (1H, dd, $J = 15.5, 9.2$ Hz, H-2a), 2.40 (1H, dd, $J = 15.5, 4.3$ Hz, H-2b), 2.38 (1H, bdd, $J = 14.1, 7.8$

Hz, H-14b), 2.11 (3H, d, $J = 1.3$ Hz, H-27), 1.96 (1H, m, H-8), 1.33 (3H, s, H-23), 1.11 (3H, d, $J = 6.9$ Hz, H-24), 1.06 (3H, s, H-22), 1.05 (3H, d, $J = 6.8$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 475 [M]⁺ (13), 387 (2), 316 (4), 288 (15), 230 (16), 204 (9), 171 (18), 168 (100), 164 (14), 151 (17); HREIMS m/z 475.2361 (calcd. for $\text{C}_{26}\text{H}_{37}\text{NO}_5\text{S}$, 475.2392).

5 [0021] Epothilone **C₇** (25): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c 2.0, MeOH); UV (MeOH) λ_{max} nm (ε) XXX (XXX), XXX (XXX); IR (KBr) ν_{max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.01 (1H, s, H-19), 6.66 (1H, bs, H-17), 5.59 (1H, ddd, $J = 11.1, 11.1, 3.8$ Hz, H-12), 5.40 (1H, dd, $J = 11.1, 9.2$, H-13), 5.03 (1H, d, $J = 9.3$ Hz, H-15), 4.62 (1H, dd, $J = 9.3, 9.2$ Hz, H-14), 4.18 (1H, bd, $J = 11.0$ Hz, H-3), 3.72 (1H, bs, H-7), 3.20 (1H, bs, 3-OH), 3.09 (1H, dq, $J = 1.9, 6.8$ Hz, H-6), 3.00 (1H, bs, 7-OH), 2.69 (3H, s, H-21), 2.47 (1H, dd, $J = 14.8, 11.0$ Hz, H-2a), 2.32 (1H, dd, $J = 14.8, 2.6$ Hz, H-2b), 2.27 (1H, m, H-11a), 2.19 (3H, bs, H-27), 2.13 (1H, m, H-11b), 1.76 (1H, m, H-8), 1.70 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.32 (3H, s, H-23), 1.23 (1H, m, H-9b), 1.21 (1H, m, H-10b), 1.18 (3H, d, $J = 6.8$ Hz, H-24), 1.08 (3H, s, H-22), 1.00 (3H, d, $J = 6.9$ Hz, H-25); EIMS m/z 493 [M]⁺ XXX; HREIMS m/z 493.XXX (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$, 493.2498).

10 [0022] Epothilone **C₈** (26): colorless amorphous solid; $[\alpha]_D^{22}$ -75.2 (c 2.5, MeOH); UV (MeOH) λ_{max} nm (ε) 210 (16800), 248 (17800); IR (KBr) ν_{max} 3443, 2932, 2881, 1734, 1689, 1465, 1255, 1183, 976 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.93 (1H, s, H-19), 6.62 (1H, dd, $J = 15.6, 0.6$ Hz, H-17), 6.49 (1H, dd, $J = 15.6, 6.6$ Hz, H-16), 5.52 (1H, dddd, $J = 9.5, 6.6, 2.8, 0.6$ Hz, H-15), 5.42 (1H, m, H-12), 5.41 (1H, m, H-13), 4.13 (1H, ddd, $J = 11.0, 5.3, 2.8$ Hz, H-3), 3.69 (1H, ddd, $J = 3.7, 2.8, 2.5$ Hz, H-7), 3.11 (1H, dq, $J = 2.5, 6.8$ Hz, H-6), 2.95 (1H, d, $J = 5.3$ Hz, 3-OH), 2.90 (1H, d, $J = 2.8$ Hz, 7-OH), 2.69 (3H, s, H-21), 2.67 (1H, ddd, $J = 14.9, 9.5, 8.4$ Hz, H-14a), 2.48 (1H, dd, $J = 15.6, 11.0$ Hz, H-2a), 2.33 (1H, dd, $J = 15.6, 2.8$ Hz, H-2b), 2.30 (1H, bd, $J = 14.9$ Hz, H-14b), 2.14 (1H, m, H-11a), 2.03 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.31 (1H, m, H-9a), 1.29 (3H, s, H-23), 1.17 (3H, d, $J = 6.8$ Hz, H-24), 1.16 (1H, m, H-10b), 1.14 (1H, m, H-9b), 1.05 (3H, s, H-22), 0.97 (3H, d, $J = 7.1$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 [M]⁺ (21), 310 (10), 276 (21), 171 (83), 154 (100), 150 (27), 111 (18); HREIMS m/z 463.2382 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

25 [0023] Epothilone **C₉** (27): colorless amorphous solid; $[\alpha]_D^{22}$ -93.4 (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ε) 209 (15200), 254 (15700); IR (KBr) ν_{max} 3416, 2966, 2932, 1736, 1689, 1463, 1249, 1011 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.06 (1H, s, H-19), 6.65 (1H, bs, H-17), 6.56 (1H, dd, $J = 10.6, 4.4$ Hz, 27-OH), 5.55 (1H, d, $J = 6.2$ Hz, 3-OH), 5.52 (1H, dd, $J = 11.6, 2.0$ Hz, H-15), 5.44 (1H, dddd, $J = 11.2, 10.7, 3.1, 1.7$ Hz, H-12), 5.35 (1H, dddd, $J = 11.0, 10.7, 3.9, 1.7$ Hz, H-13), 4.47 (1H, ddd, $J = 12.5, 4.4, 1.3$ Hz, H-27a), 4.35 (1H, ddd, $J = 11.7, 6.2, 2.6$ Hz, H-3), 4.20 (1H, ddd, $J = 12.5, 10.6, 0.9$ Hz, H-27b), 3.63 (1H, ddd, $J = 4.6, 1.8, 0.9$ Hz, H-7), 3.24 (1H, d, $J = 1.8$ Hz, 7-OH), 3.13 (1H, dq, $J = 0.9, 6.8$ Hz, H-6), 2.80 (1H, ddd, $J = 14.8, 11.6, 11.0$ Hz, H-14a), 2.71 (3H, s, H-21), 2.40 (1H, dd, $J = 14.4, 11.7$ Hz, H-2a), 2.24 (1H, m, H-11a), 2.06 (1H, dd, $J = 14.4, 2.6$ Hz, H-2b), 2.01 (1H, ddd, $J = 14.8, 3.9, 2.0$ Hz, H-14b), 2.00 (1H, m, H-11b), 1.77 (1H, m, H-8), 1.69 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.35 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.19 (3H, d, $J = 6.8$ Hz, H-24), 1.18 (1H, m, H-9b), 1.01 (3H, d, $J = 7.1$ Hz, H-25), 0.98 (3H, s, H-22); ^{13}C NMR, see Table 1; EIMS m/z 493 [M]⁺ (17), 306 (64), 184 (50), 171 (30), 167 (38), 166 (100), 138 (12); HREIMS m/z 493.2502 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$, 493.2498).

30 [0024] trans-Epothilone **C₁** (28): colorless amorphous solid; $[\alpha]_D^{22}$ -84 (c 0.2, MeOH); UV (MeOH) λ_{max} nm (ε) 211 (17400), 248 (12900); IR (KBr) ν_{max} 3433, 2961, 2933, 2879, 1730, 1708, 1457, 1251, 975 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.00 (1H, s, H-19), 6.64 (1H, bs, H-17), 5.45 (1H, ddd, $J = 15.2, 6.5, 6.5$ Hz, H-12), 5.42 (1H, dd, $J = 6.4, 3.7$ Hz, H-15), 5.35 (1H, dt, $J = 15.2, 7.1$ Hz, H-13), 4.42 (1H, m, H-3), 3.58 (1H, ddd, $J = 8.1, 7.9, 2.8$ Hz, H-7), 3.24 (1H, m, H-6), 3.14 (1H, dq, $J = 4.0, 6.9$ Hz, H-6), 2.92 (1H, d, $J = 7.9$ Hz, 7-OH), 2.71 (3H, s, H-21), 2.71 (2H, m, H-2), 2.53 (2H, m, H-14), 2.17 (1H, d, $J = 2.17$ Hz, 3-OH), 2.11 (1H, m, H-11a), 2.06 (3H, bs, H-27), 1.93 (1H, m, H-11b), 1.68 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-8), 1.26 (3H, d, $J = 6.8$ Hz, H-24), 1.16 (1H, m, H-10b), 1.12 (3H, d, $J = 6.9$ Hz, H-22), 1.07 (1H, m, H-9b), 1.00 (3H, d, $J = 6.8$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 [M]⁺ (6), 290 (21), 289 (20), 204 (23), 194 (19), 190 (22), 168 (100), 164 (48), 157 (14), 152 (19), 151 (17), 139 (15), 111 (18); HREIMS m/z 463.2371 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

45 [0025] trans-Epothilone **C₂** (29): colorless amorphous solid; $[\alpha]_D^{22}$ -3 (c 1.5, MeOH); UV (MeOH) λ_{max} nm (ε) 211 (15800), 248 (11900); IR (KBr) ν_{max} 3435, 2963, 2931, 2878, 1731, 1706, 1457, 1273, 979 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 6.99 (1H, s, H-19), 6.57 (1H, bs, H-17), 5.56 (1H, ddd, $J = 15.1, 7.4, 7.0$ Hz, H-12), 5.41 (1H, ddd, $J = 15.1, 7.0, 6.9$ Hz, H-13), 5.41 (1H, dd, $J = 7.7, 2.8$ Hz, H-15), 4.13 (1H, dddd, $J = 6.7, 6.2, 5.6, 5.1$ Hz, H-3), 3.78 (1H, ddd, $J = 8.2, 6.5, 1.9$ Hz, H-7), 3.18 (1H, d, $J = 5.6$ Hz, 3-OH), 3.06 (1H, dq, $J = 8.2, 7.1$ Hz, H-6), 2.98 (1H, dq, $J = 6.2, 7.0$ Hz, H-4), 2.71 (3H, s, H-21), 2.64 (1H, dd, $J = 15.1, 6.7$ Hz, H-2a), 2.54 (1H, dd, $J = 15.1, 5.1$ Hz, H-2b), 2.44 (2H, m, H-14), 2.22 (1H, dddd, $J = 13.8, 7.0, 6.2, 2.9$ Hz, H-11a), 2.10 (3H, d, $J = 1.1$ Hz, H-27), 2.09 (1H, d, $J = 6.5$ Hz, 7-OH), 1.88 (1H, dddd, $J = 13.8, 10.9, 7.4, 2.9$ Hz, H-11b), 1.65 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.56 (1H, dddd, $J = 12.7, 12.7, 3.9, 3.9$ Hz, H-9a), 1.20 (3H, d, $J = 7.1$ Hz, H-24), 1.15 (3H, d, $J = 7.0$ Hz, H-23), 1.13 (1H, m, H-10b), 1.04 (1H, m, H-9b), 1.01 (3H, d, $J = 7.0$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 [M]⁺ (13), 290 (11), 190 (10), 168 (100), 164 (20), 157 (26), 139 (17); HREIMS m/z 463.2383 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

[0026] Epothilone **I₁** (30): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{max} nm (ε) XXX;

- IR (KBr) ν_{\max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.96 (1H, s, H-19), 6.54 (1H, bs, H-17), 5.49 (1H, ddd, $J = 10.3$, 7.3, 7.3 Hz, H-12), 5.33 (1H, dd, $J = 8.3$, 4.4 Hz, H-15), 5.31 (1H, m, H-13), 4.15 (1H, ddd, $J = 8.0$, 5.0, 4.6 Hz, H-3), 3.80 (1H, m, H-7), 3.21 (1H, dq, $J = 6.0$, 6.9 Hz, H-6), 2.89 (1H, d, $J = 5.0$ Hz, 3-OH); 2.70 (3H, s, H-21), 2.65 (1H, ddd, $J = 15.8$, 8.5, 8.3 Hz, H-14a), 2.42 (2H, m, H-2), 2.35 (1H, m, H-14b), 2.27 (1H, bd, $J = 3.3$ Hz, 7-OH), 2.13 (1H, m, H-11a), 2.09 (3H, d, $J = 1.2$ Hz, H-27), 2.00 (1H, m, H-11b), 1.72 (1H, m, H-8), 1.40 (2H, m, H-10_β), 1.37 (1H, m, H-9_βa), 1.36 (2H, m, H-9_α), 1.32 (3H, s, H-23), 1.27 (3H, m, H-9_βb and H-10_α), 1.13 (3H, d, $J = 6.9$ Hz, H-24), 1.09 (3H, s, H-22), 0.94 (3H, d, $J = 6.9$ Hz, H-25); ^{13}C NMR (CDCl_3 , 75 MHz) δ 221.3 (s, C-5), 171.1 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.4 (s, C-16), 133.8 (d, C-12), 124.6 (d, C-13), 120.0 (d, C-17), 116.2 (d, C-19), 78.8 (d, C-15), 74.9 (d, C-7), 74.7 (d, C-3), 51.6 (s, C-4), 43.7 (d, C-6), 38.9 (t, C-2), 34.3 (d, C-8), 31.6 (t, C-14), 29.3 (t, C-9_α), 28.6 (t, C-10_β), 28.2 (t, C-10_α), 26.6 (t, C-11), 24.8 (t, C-9_β), 23.6 (q, C-22), 19.3 (q, C-23), 19.3 (q, C-21), 16.5 (q, C-25), 15.5 (q, C-27), 13.7 (q, C-24); EIMS m/z 505 $[\text{M}]^+$ XXX; HREIMS m/z 505.XXX (calcd. for $\text{C}_{28}\text{H}_{43}\text{NO}_5\text{S}$, 505.XXX).
- [0027] Epothilone I₂ (31): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{\max} nm (ε) XXX; IR (KBr) ν_{\max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.40 (1H, m, H-12), 5.38 (1H, dd, $J = 9.8$, 3.3 Hz, H-15), 5.37 (1H, m, H-13), 4.21 (1H, ddd, $J = 8.6$, 3.8, 3.6 Hz, H-3), 3.85 (1H, ddd, $J = 8.5$, 5.8, 2.2 Hz, H-7), 3.18 (1H, dq, $J = 8.5$, 7.0 Hz, H-6), 2.70 (3H, s, H-21), 2.65 (1H, ddd, $J = 15.2$, 9.8, 9.0 Hz, H-14a), 2.51 (1H, d, $J = 3.6$ Hz, 3-OH), 2.37 (2H, m, H-2), 2.32 (1H, bd, $J = 15.2$ Hz, H-14b), 2.09 (3H, d, $J = 1.3$ Hz, H-27), 2.07 (2H, m, H-11), 1.78 (1H, m, H-8), 1.65 (1H, d, $J = 5.8$ Hz, 7-OH), 1.57 (1H, m, H-10_βa), 1.44 (1H, m, H-10_αa), 1.42 (1H, m, H-9_β), 1.32 (3H, s, H-23), 1.21 (1H, m, H-10_βb), 1.17 (3H, d, $J = 7.0$ Hz, H-24), 1.13 (2H, m, H-9_α), 1.06 (3H, s, H-22), 0.95 (3H, d, $J = 7.0$ Hz, H-25_α), 0.91 (3H, d, $J = 6.5$ Hz, H-25_β), 0.68 (1H, m, H-10_αb); ^{13}C NMR (CDCl_3 , 100 MHz) δ 220.4 (s, C-5), 171.3 (s, C-1), XXX (s, C-20), 152.4 (s, C-18), 137.6 (s, C-16), 134.5 (d, C-12), 125.3 (d, C-13), 119.6 (d, C-17), 116.2 (d, C-19), 78.6 (d, C-15), 77.2 (d, C-7), 75.0 (d, C-3), 51.0 (s, C-4), 44.6 (d, C-6), 38.2 (t, C-2), 36.9 (t, C-9_α), 34.5 (t, C-10_α), 32.6 (d, C-8), 32.0 (t, C-14), 30.0 (d, C-9_β), 27.4 (t, C-11), 26.6 (t, C-10_β), 25.0 (q, C-22), 21.5 (q, C-25_β), 19.3 (q, C-21), 17.9 (q, C-25_α), 17.7 (q, C-23), 15.8 (q, C-24), 15.6 (q, C-27); EIMS m/z 519 $[\text{M}]^+$ XXX; HREIMS m/z 519.XXX (calcd. for $\text{C}_{29}\text{H}_{45}\text{NO}_5\text{S}$, 519.XXX).
- [0028] Epothilone I₃ (32): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{\max} nm (ε) XXX; IR (KBr) ν_{\max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.95 (1H, s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd, $J = 9.1$, 3.0 Hz, H-15), 5.08 (1H, dd, $J = 8.5$, 3.9 Hz, H-13), 4.13 (1H, ddd, $J = 9.4$, 4.3, 3.2 Hz, H-3), 3.81 (1H, m, H-7), 3.18 (1H, dq, $J = 6.8$, 7.0 Hz, H-6), 2.83 (1H, d, $J = 4.3$ Hz, 3-OH), 2.70 (3H, s, H-21), 2.61 (1H, ddd, $J = 15.8$, 9.1, 8.5 Hz, H-14a), 2.43 (1H, dd, $J = 14.0$, 3.2 Hz, H-2a), 2.38 (2H, dd, $J = 14.0$, 9.4 Hz, H-2b), 2.30 (1H, bd, $J = 15.8$ Hz, H-14b), 2.16 (1H, ddd, $J = 14.1$, 8.3, 7.4 Hz, H-11a), 2.08 (3H, d, $J = 1.0$ Hz, H-27), 1.99 (1H, d, $J = 4.7$ Hz, 7-OH), 1.92 (1H, ddd, $J = 14.1$; 6.3, 6.3 Hz, H-11b), 1.82 (1H, m, H-8), 1.67 (3H, s, H-26), 1.51 (1H, m, H-10_βa), 1.40 (1H, m, H-9_β), 1.33 (1H, m, H-10_βb), 1.31 (3H, s, H-23), 1.27 (1H, m, H-10_αa), 1.23 (1H, m, H-9_αa), 1.16 (3H, d, $J = 7.0$ Hz, H-24), 1.10 (1H, m, H-9_αb), 1.07 (3H, s, H-22), 0.95 (3H, d, $J = 7.0$ Hz, H-25_α), 0.92 (3H, d, $J = 6.5$ Hz, H-25_β), 0.75 (1H, m, H-10_αb); EIMS m/z 533 $[\text{M}]^+$ XXX; HREIMS m/z 533.XXX (calcd. for $\text{C}_{30}\text{H}_{47}\text{NO}_5\text{S}$, 533.XXX).
- [0029] Epothilone I₄ (33): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{\max} nm (ε) XXX; IR (KBr) ν_{\max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.47 (1H, dd, $J = 11.1$, 5.8 Hz, H-12), 5.33 (1H, ddd, $J = 9.2$, 3.9, 0.5 Hz, H-15), 5.33 (1H, m, H-13), 4.09 (1H, dddd, $J = 9.6$, 8.1, 4.5, 3.3 Hz, H-3), 3.83 (1H, m, H-7), 3.57 (1H, bs, 3-OH), 2.89 (1H, dq, $J = 7.4$, 7.1 Hz, H-6), 2.83 (1H, dq, $J = 8.1$, 7.1 Hz, H-4), 2.70 (3H, s, H-21), 2.64 (1H, m, H-14a), 2.42 (1H, dd, $J = 14.2$, 3.3 Hz, H-2a), 2.43 (1H, dd, $J = 14.2$, 9.6 Hz, H-2b), 2.30 (1H, m, H-14b), 2.10 (3H, d, $J = 1.3$ Hz, H-27), 2.09 (2H, m, H-11), 1.81 (1H, m, H-8), 1.74 (1H, bd, $J = 5.6$ Hz, 7-OH), 1.53 (1H, m, H-10_βa), 1.49 (1H, m, H-9_β), 1.47 (1H, m, H-10_αa), 1.27 (1H, m, H-10_βb), 1.24 (1H, m, H-9_αa), 1.17 (3H, d, $J = 7.1$ Hz, H-23), 1.14 (1H, m, H-9_αb), 1.08 (3H, d, $J = 7.1$ Hz, H-24), 0.97 (3H, d, $J = 6.9$ Hz, H-25_α), 0.91 (3H, d, $J = 6.5$ Hz, H-25_β), 0.79 (1H, m, H-10_αb); ^{13}C NMR (CDCl_3 , 100 MHz) δ 217.0 (s, C-5), 170.8 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.1 (s, C-16), 134.6 (d, C-12), 124.7 (d, C-13), 120.2 (d, C-17), 116.4 (d, C-19), 78.7 (d, C-15), 76.4 (d, C-7), 71.3 (d, C-3), 50.7 (d, C-4), 50.1 (d, C-6), 40.7 (t, C-2), 38.5 (t, C-9_α), 35.5 (t, C-10_α), 33.4 (d, C-8), 31.8 (t, C-14), 30.0 (d, C-9_β), 27.2 (t, C-11), 26.7 (t, C-10_β), 21.4 (q, C-25_β), 19.3 (q, C-21), 18.2 (q, C-25_α), 15.4 (q, C-27), 14.4 (q, C-24), 13.1 (q, C-23); EIMS m/z 505 $[\text{M}]^+$ XXX; HREIMS m/z 505.XXX (calcd. for $\text{C}_{28}\text{H}_{43}\text{NO}_5\text{S}$, 505.XXX).
- [0030] Epothilone I₅ (34): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{\max} nm (ε) XXX; IR (KBr) ν_{\max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.97 (1H, s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd, $J = 7.1$, 6.2 Hz, H-15), 5.03 (1H, dd, $J = 8.4$, 5.0 Hz, H-13), 4.05 (1H, dddd, $J = 7.5$, 7.2, 5.9, 4.6 Hz, H-3), 3.91 (1H, m, H-7), 3.17 (1H, d, $J = 5.9$ Hz, 3-OH), 2.94 (1H, dq, $J = 7.2$, 7.1 Hz, H-4), 2.87 (1H, dq, $J = 6.5$, 6.9 Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd, $J = 14.6$, 4.6 Hz, H-2a), 2.60 (1H, m, H-14a), 2.53 (1H, dd, $J = 14.6$, 7.5 Hz, H-2b), 2.31 (1H, m, H-14b), 2.10 (3H, d, $J = 1.1$ Hz, H-27), 2.10 (1H, m, H-11a), 2.02 (1H, m, H-11b), 1.97 (1H, bd, $J = 5.6$ Hz, 7-OH), 1.84 (1H, m, H-8), 1.66 (3H, s, H-26), 1.55 (1H, m, H-9_β), 1.49 (1H, m, H-10_βa), 1.39 (1H, m, H-10_βb), 1.33 (1H, m, H-10_αa), 1.31 (1H, m, H-9_αa), 1.15 (3H, d, $J = 7.1$ Hz, H-23), 1.12 (1H, m, H-9_αb), 1.11 (3H, d, $J = 6.9$ Hz, H-24), 0.97 (3H, d, $J = 6.9$ Hz, H-25_α), 0.94 (1H, m, H-10_αb), 0.93 (3H, d, $J = 6.6$ Hz, H-25_β); EIMS m/z 519 $[\text{M}]^+$ XXX; HREIMS m/z 519.XXX (calcd. for $\text{C}_{29}\text{H}_{45}\text{NO}_5\text{S}$, 519.XXX).

- [0031] Epothilone I₆ (35): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{\max} nm (e) XXX; IR (KBr) ν_{\max} XXX cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 6.97 (1H, s, H-19), 6.52 (1H, bs, H-17), 5.24 (1H, dd, J = 6.9, 6.9 Hz, H-15), 5.02 (1H, dd, J = 8.8, 5.2 Hz, H-13), 4.22 (1H, tdd, J = 6.1, 5.6, 4.8 Hz, H-3), 3.76 (1H, ddd, J = 6.1, 5.7, 5.6 Hz, H-7), 3.13 (1H, d, J = 5.6 Hz, 3-OH), 3.05 (1H, dq, J = 4.8, 7.0 Hz, H-4), 2.79 (1H, dq, J = 5.6, 6.9 Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, m, H-14a), 2.57 (2H, d, J = 6.1 Hz, H-2a), 2.30 (1H, m, H-14b), 2.08 (3H, d, J = 1.0 Hz, H-27), 2.02 (2H, m, H-11), 1.73 (1H, d, J = 6.1 Hz, 7-OH), 1.69 (1H, m, H-8), 1.66 (3H, s, H-26), XXX (H-9_α, H-9_β, H-10_α, H-10_β), 1.21 (3H, d, J = 7.0 Hz, H-22), 1.16 (3H, d, J = 6.9 Hz, H-24), 0.94 (3H, d, J = 6.9 Hz, H-25_α), 0.91 (3H, d, J = 6.4 Hz, H-25_β); EIMS *m/z* 519 [M]⁺ XXX; HREIMS *m/z* 519.XXX (calcd. for C₂₉H₄₅NO₅S, 519.XXX).
- [0032] Epothilone K (36): colorless amorphous solid; $[\alpha]_D^{22}$ -7 (c 0.08, MeOH); UV (MeOH) λ_{\max} nm (e) 212 (16700), 248 (12500); IR (KBr) ν_{\max} 3431, 2963, 2927, 2856, 1731, 1712, 1262, 1093, 1021, 802 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 6.95 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.49 (3H, m, H-15, H-13, and H-12), 4.04 (1H, dddd, J = 7.9, 7.6, 6.9, 3.3 Hz, H-3), 3.36 (1H, dq, J = 6.9, 6.8 Hz, H-6), 2.83 (1H, d, J = 7.6 Hz, 3-OH), 2.75 (1H, ddd, J = 16.1, 6.6, 3.4 Hz, H-14a), 2.74 (1H, dd, J = 15.3, 3.3 Hz, H-2a), 2.71 (3H, s, H-21), 2.58 (2H, m, H-14b and H-8), 2.50 (1H, dd, J = 15.3, 7.9 Hz, H-2b), 2.29 (1H, m, H-11a), 2.10 (1H, m, H-11b), 2.09 (3H, d, J = 0.7 Hz, H-27), 1.78 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.48 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.15 (3H, d, J = 6.8 Hz, H-22), 1.03 (3H, d, J = 6.5 Hz, H-25); EIMS *m/z* 405 [M]⁺ (38), 317 (12), 260 (9), 232 (10), 204 (14), 190 (16), 168 (100), 164 (30), 151 (28); HREIMS *m/z* 405.XXX (calcd. for C₂₆H₃₉NO₅S, 405.XXX).
- [0033] (37): colorless amorphous solid; $[\alpha]_D^{22}$ -27.5 (c 0.4, MeOH); UV (MeOH) λ_{\max} nm (e) 211 (16100), 247 (12100); IR (KBr) ν_{\max} 3431, 2967, 2929, 2875, 1704, 1462, 1381, 1010 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.56 (1H, dt, J = 10.8, 7.3, 1.4 Hz, H-12), 5.39 (1H, dt, J = 10.8, 7.3, 1.4 Hz, H-13), 4.17 (1H, t, J = 6.6 Hz, H-15), 3.50 (1H, ddd, J = 8.7, 2.6, 2.6 Hz, H-7), 3.10 (1H, d, J = 2.6, 7-OH), 2.90 (1H, dq, J = 2.6, 7.2 Hz, H-6), 2.77 (1H, sep, J = 6.9 Hz, H-4), 2.70 (3H, s, H-21), 2.40 (2H, m, H-14), 2.07 (2H, m, H-11), 2.04 (3H, d, J = 1.1 Hz, H-27), 1.78 (1H, bs, 15-OH), 1.74 (1H, m, H-9a), 1.50 (1H, m, H-8), 1.46 (1H, m, H-10a), 1.27 (1H, m, H-10b), 1.11 (1H, m, H-9b), 1.094 (3H, d, J = 6.9 Hz, H-23), 1.089 (3H, d, J = 6.9 Hz, H-22), 1.08 (3H, d, J = 7.2 Hz, H-24), 0.82 (3H, d, J = 6.7 Hz, H-25); ¹³C NMR (CDCl₃, 100 MHz) δ 220.5 (s, C-5), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 133.4 (d, C-12), 125.0 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 74.9 (d, C-7), 44.9 (d, C-6), 40.0 (d, C-4), 35.5 (d, C-8), 33.5 (t, C-14), 32.3 (t, C-9), 27.9 (t, C-11), 26.9 (t, C-10), 19.2 (q, C-21), 18.6 (q, C-23), 18.1 (q, C-22), 15.6 (q, C-25), 14.4 (q, C-27), 9.3 (q, C-24); EIMS *m/z* 407 [M]⁺ (0.1), 204 (0.8), 168 (100), 140 (3.4); HREIMS *m/z* 407.XXX (calcd. for C₂₃H₃₇NO₅S, 407.XXX).
- [0034] (38): colorless amorphous solid; $[\alpha]_D^{22}$ +25.0 (c 0.5, MeOH); UV (MeOH) λ_{\max} nm (e) 212 (17700), 247 (13400); IR (KBr) ν_{\max} 3427, 2971, 2933, 2878, 2858, 1709, 1457, 1377, 1186, 1023 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 6.95 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.52 (1H, dt, J = 10.9, 7.2, 1.4 Hz, H-12), 5.39 (1H, dt, J = 10.9, 7.1, 1.2 Hz, H-13), 4.18 (1H, ddt, J = 3.4, 0.4, 6.7 Hz, H-15), 2.71 (3H, s, H-21), 2.51 (1H, bq, J = 6.8 Hz, H-8), 2.48 (1H, dq, J = 17.7, 7.4 Hz, H-6a), 2.41 (1H, dq, J = 17.7, 7.2 Hz, H-6b), 2.39 (2H, ddd, J = 7.1, 6.7, 1.4 Hz, H-14), 2.06 (2H, ddt, J = 7.2, 1.2, 7.0 Hz, H-11), 2.05 (3H, d, J = 1.4 Hz, H-27), 1.81 (1H, d, J = 3.4 Hz, 15-OH), 1.66 (1H, m, H-9a), 1.32 (1H, m, H-9b), 1.31 (2H, m, H-10), 1.06 (3H, d, J = 6.9 Hz, H-25), 1.04 (3H, dd, J = 7.4, 7.2 Hz, H-24); ¹³C NMR (CDCl₃, 75 MHz) δ 215.3 (s, C-7), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 132.7 (d, C-12), 125.3 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 46.0 (d, C-8), 34.3 (t, C-14), 33.5 (t, C-6), 32.7 (t, C-9), 27.5 (t, C-11), 27.3 (t, C-10), 19.2 (q, C-21), 16.5 (q, C-25), 14.4 (q, C-27), 7.8 (q, C-24); EIMS *m/z* 335 [M]⁺ (2), 317 (4), 170 (27), 169 (67), 168 (100), 140 (20); HREIMS *m/z* 335.1912 (calcd. for C₁₉H₂₉NO₂S, 335.1919).
- [0035] (39): colorless amorphous solid; $[\alpha]_D^{22}$ +26.4 (c 0.27, MeOH); UV (MeOH) λ_{\max} nm (e) 203 (19100), 244 (12500); IR (KBr) ν_{\max} 3430, 2970, 2934, 2877, 1710, 1458, 1377, 1184 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.17 (1H, t, J = 7.3 Hz, H-13), 4.13 (1H, m, H-15), 2.70 (3H, s, H-21), 2.51 (1H, bq, J = 6.8 Hz, H-8), 2.47 (1H, dq, J = 17.7, 7.2 Hz, H-6a), 2.41 (1H, dq, J = 17.7, 7.2 Hz, H-6b), 2.33 (2H, bdd, J = 7.3, 6.8 Hz, H-14), 2.05 (3H, d, J = 1.2 Hz, H-27), 2.03 (2H, m, H-11), 1.71 (1H, d, J = 3.2 Hz, 15-OH), 1.69 (3H, d, J = 1.3 Hz, H-26), 1.62 (1H, in, H-9a), 1.32 (3H, m, H-10 and H-9b), 1.06 (3H, d, J = 6.9 Hz, H-25), 1.03 (3H, t, J = 7.2 Hz, H-24); EIMS *m/z* 349 [M]⁺ (0.7), 331 (1.7), 168 (100), 140 (5.1); HREIMS *m/z* 349.XXX (calcd. for C₂₀H₃₁NO₂S, 349.XXX).

Tab 1.

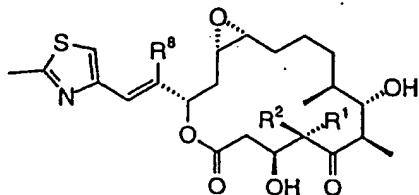
Struktur-typ	Epothilone				
	A _Y	B _Y	C _Y	D _Y	trans C _Y
Ausgangsepothilon	(1) 4	(2) 1-2	(14) 50-100	(15) 20	-
21-Hydroxy (E&F)	(3) 10	(4) 1.5	-	-	-
Oxazoles (G&H)	(10) 6	(11) 1	(12) 120	(13) 11	-

Tab 1. (fortgesetzt)

Aktivität von Epothilonen und Verbindungen (1) bis (39) gegen Maus-Fibroblasten (L929, IC50 /ng/ml)					
Struktur-typ	Epothilone				
	A _Y	B _Y	C _Y	D _Y	trans C _Y
Ausgangsepothilon	(1) 4	(2) 1-2	(14) 50-100	(15) 20	-
(R)-4-Desmethyl (X ₁)	(5) 20	-	(16) 200	(17) 20	(28) 400
(S)-4-Desmethyl (X ₂)	(6) 7	-	(18) 25-30	(19) 12	(29) 80
6-Desmethyl (X ₃)	-	-	(20) 1500	-	-
8-Desmethyl (X ₄)	-	-	(21) 800	-	-
8,9-Dehydro (X ₅)	-	-	(22) 1500	(23) 200	-
10,11-Dehydro (X ₆)	-	-	(24) 120	-	-
14-Hydroxy (X ₇)	-	-	(25)	-	-
16-Desmethyl (X ₈)	(7) 20	-	(26) 250	-	-
27-Hydroxy (X ₉)	(8) 100	-	(27) 200	-	-
21-Methyl (X ₁₀)	-	(9) 1.5	-	-	-
Verbindung	-	-	(36) 180	-	-
Verbindung	-	-	(37) 50	-	-
Verbindung	-	-	(38) 2000	(39) 500	-

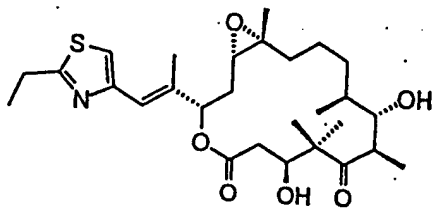
Patentansprüche

1. Epothilon der Formel



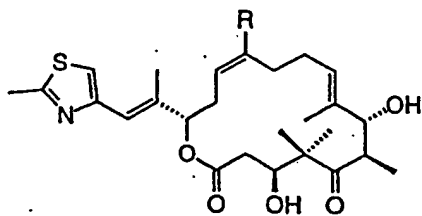
Epothilone A₉ (8) R¹ = CH₂OH; R², R⁸ = Me

2. Epothilon der Formel



Epothilone B₁₀ (9)

3. Epothilon der Formel

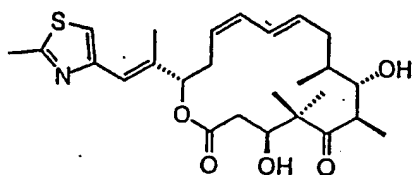


Epothilone C₅ (22) R = H

Epothilone D₅ (23) R = Me.

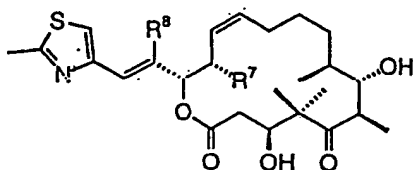
oder

4. Epothilon der Formel



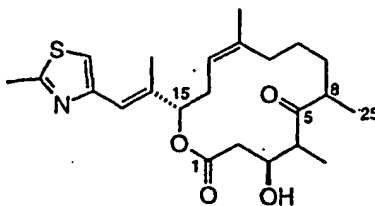
Epothilone C₆ (24)

5. Epothilon der Formel



Epothilone C₉ (27) R⁸ = CH₂OH; R⁷ = H

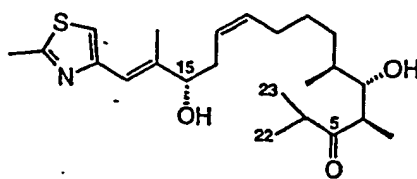
6. Epothilon der Formel



Epothilone K (36)

7. Verbindung der Formel

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(37)

Fig. 1

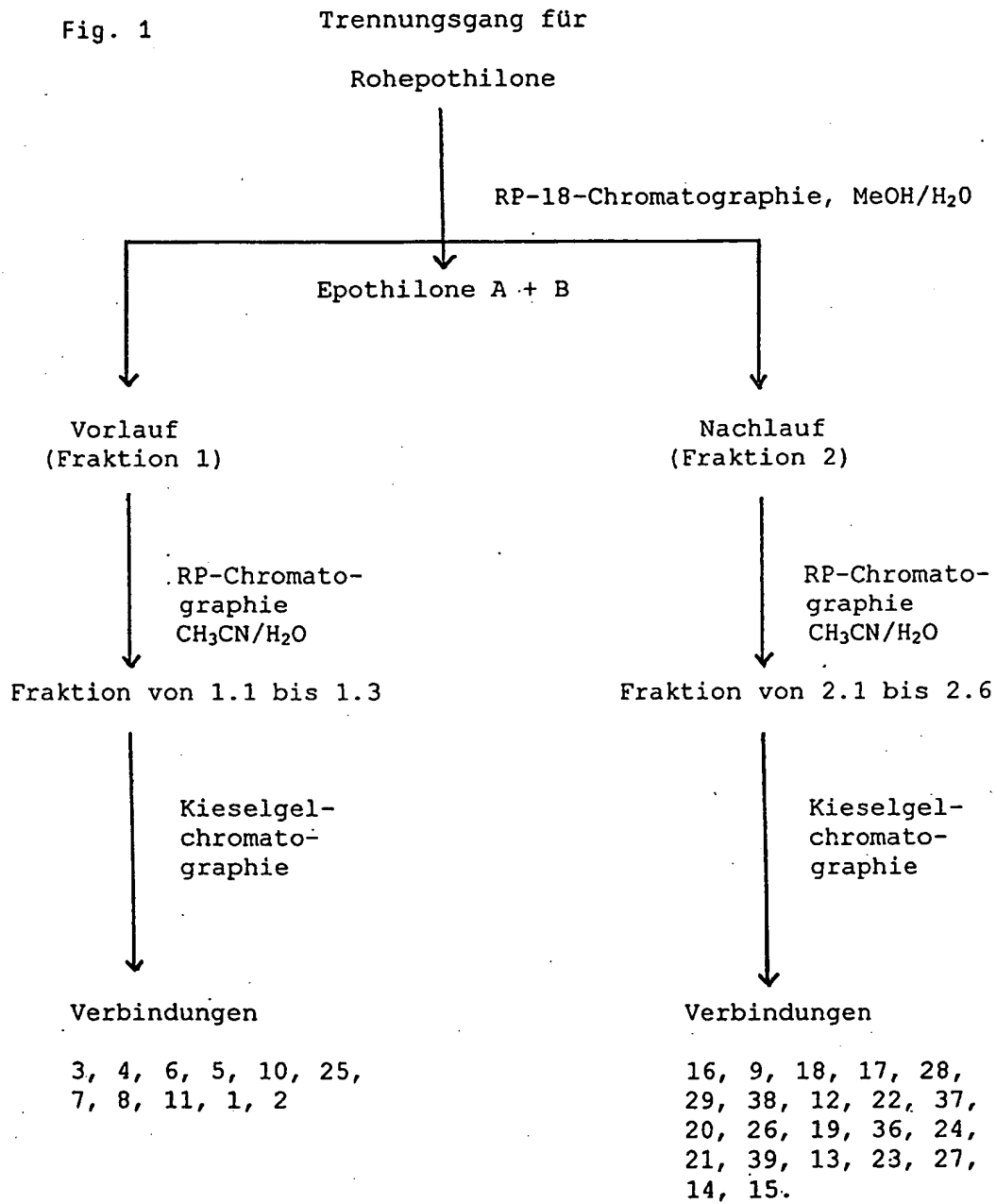


Fig. 2

2

fraction 1	1.1	Epothilone E (3)	variable ^a
		Epothilone F (4)	variable ^a
		Epothilone A ₂ (6)	14.5 mg
		Epothilone A ₁ (5)	3.1 mg
		Epothilone G ₁ (10)	52.3 mg
	1.2	Epothilone C ₇ (25)	0.9 mg
		Epothilone A ₈ (7)	38.7 mg
	1.3	Epothilone A ₉ (8)	4.4 mg
		Epothilone G ₂ (11)	9.4 mg
	fraction 2		Epothilone A (1)
		Epothilone B (2)	10300.0 mg
2.1		Epothilone C ₁ (16)	32.4 mg
		Epothilone B ₁₀ (9)	1.1 mg
2.2		Epothilone C ₂ (18)	58.4 mg
2.3		Epothilone D ₁ (17)	5.3 mg
		trans-Epothilone C ₁ (28)	1.4 mg
		trans-Epothilone C ₂ (29)	4.5 mg
		38	6.5 mg
		Epothilone H ₁ (12)	3.0 mg
		Epothilone C ₈ (22)	7.3 mg
2.4		37	2.9 mg
		Epothilone C ₃ (20)	32.5 mg
		Epothilone C ₆ (26)	26.3 mg
		Epothilone D ₂ (19)	13.1 mg
		Epothilone K (36)	0.4 mg
2.5		Epothilone C ₉ (24)	2.9 mg
		Epothilone C ₄ (21)	6.5 mg
		39	0.8 mg
2.6		Epothilone H ₂ (13)	1.5 mg
		Epothilone D ₃ (23)	0.9 mg
		Epothilone C ₅ (27)	3.0 mg
		Epothilone C (14)	4600.0 mg
		Epothilone D (15)	2700.0 mg



Europäisches
Patentamt

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Nummer der Anmeldung
EP 02 02 2332

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Recherchenort	Abschlußdatum der Recherche	Prüfer	
DEN HAAG	21. November 2002	Chouly, J	
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EP 02 02 2332

In diesem Anhang sind die Mitglieder der Patentfamilien der im obengenannten europäischen Recherchenbericht angeführten Patentdokumente angegeben.
Die Angaben über die Familienmitglieder entsprechen dem Stand der Datei des Europäischen Patentamts am 21-11-2002.
Diese Angaben dienen nur zur Unterrichtung und erfolgen ohne Gewähr.

21-11-2002

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